REMARKS

Reconsideration of the present application is respectfully requested in view of the above amendments and the following remarks. Claims 1-23 were pending in the application; claims 10-19 and 21-23 have been withdrawn, and claims 1-9 and 20 are currently under examination. Notwithstanding the grounds for rejection, claims 6-8 are canceled, and claims 1-5, 9, and 20 are amended to more particularly point out and distinctly claim certain embodiments of Applicants' invention. Claim 24 has been added. Following entry of amendments, claims 1-5, 9-24 are now pending. No new matter is added by the amendments. Support for the amendments can be found in the claims as filed and in the specification, for example, on page 7, lines 1-2; page 7, lines 7-9; page 7, lines 11-14.

In addition, the specification has been amended to insert the detailed chemical formula of the presently elected compound. Support for this amendment can be found in the specification on page 1, lines 21-23, which incorporates by reference the disclosure in copending International Application PCT/AU03/00427 (*see* International Publication No. WO 2003/086386, a copy of which is enclosed). PCT/AU03/00427 describes the inserted chemical formula on page 26, referring to this formula as "compound 14." Applicants submit that the material being inserted is the material incorporated by reference, such that the amendment contains no new matter. *See* 37 C.F.R. § 1.57(f).

Claim Objections

The Examiner objects to claim 9 for the use of "μm" (i.e. micrometer) rather than "μM" (micromolar). Claim 9 has been amended to recite "μM," obviating this objection. Accordingly, Applicants respectfully request withdrawal of the objection to claim 9.

Rejection Under 35 U.S.C § 112, First Paragraph, Enablement

The Examiner rejects claims 3-4 under 35 U.S.C § 112, first paragraph, for alleged lack of enablement. The Examiner agrees that the specification enables promoting repair of UV-induced DNA mutagenic damage and/or enhancing defense against UV-induced DNA

mutagenic damage with equol, but asserts that the specification does not enable *preventing* skin cancer using the entire genus of recited compounds.

Applicants traverse this rejection and submit that the instant claims are enabled. Nonetheless, notwithstanding the rejection, claim 3 has been amended to recite "a method for *reducing* the formation of skin cancer." Support for this amendment can be found in the specification, which describes, for example, that topical application of the presently claimed compounds "*reduces*" the number of skin cancer causing CPDs following UV exposure (*see, e.g.,* page 7, lines 1-2; page 7, lines 7-9; page 7, lines 11-14). This amendment does not constitute new matter.

Applicants submit that subject matter encompassing a method of *reducing* the formation of skin cancer, such as basal cell carcinoma, squamous cell carcinoma and malignant melanoma, is commensurate in scope with the specification. Indeed, the specification discloses a relationship between cyclobutane pyrimidine dimer (CPD) formation and skin cancer, and discloses by working examples that the presently claimed compounds are capable of increasing CPD repair, thereby reducing the risk of skin cancer. Given the guidance provided in the specification, as detailed herein, a person skilled in the art can practice the subject matter of the instant claims without undue experimentation.

The specification teaches that increased CPD repair may *reduce* the risk of skin cancer formation. Specifically, the specification teaches that CPDs are an early indicator of molecular damage following UV exposure, and if not repaired, lead to fixed mutations in the DNA of skin cells (*see, e.g.,* page 12, lines 26-27). Since a person skilled in the art recognizes that these fixed mutations increase the risk of skin cancer, such a person recognizes that increased CPD repair reduces these fixed mutations, and, thus, reduces the risk of skin cancer.

In view of this understanding, the specification teaches a person skilled in the art by working examples how to routinely determine whether compounds of the recited genus increase the rate of CPD repair, and thereby reduce the risk of skin cancer. The specification describes both animal and human models to measure CPD levels following UV exposure. As one aspect of these models, CPD levels may be detected immunohistochemically using citric acid antigen retrieval and the H3 anti-pyrimidine dimer antibody (*see, e.g.,* page 6, lines 20-27).

CPD positive cells may be counted manually and compared to untreated control cells. *Id.* Utilizing such models, the specification shows empirically that equol-based compounds increase the rate of CPD repair in skin following UV exposure (*see, e.g.,* Example 1 on page 6, line 20 to page 7, line 14; and Example 3 on page 9, line 7 to page 10, line 14), and, thus, reduce the risk of skin cancer. Provided with this exemplary guidance, a person skilled in the art can *routinely* screen for compounds of the recited genus that have the recited ability to reduce skin cancer formation, such as by measuring CPD levels following UV exposure. Applicant notes that enablement is not precluded by the necessity of *routine* screening. *In re Wands* 858 F.2d 731, 736, 737 (Fed. Cir. 1988).

Given the *routine* nature of screening the recited genus of compounds for increased CPD repair, and, thus, the *routine* nature of screening for reduced skin cancer formation, as disclosed in the specification and exemplified by the working examples, a person skilled in the art can practice the full scope of the present claims without undue experimentation. Accordingly, Applicants submit that the instant claims satisfy the enablement requirement under 35 U.S.C. § 112, first paragraph, and respectfully request withdrawal of this rejection.

Rejection Under 35 U.S.C. § 112, First Paragraph, Written Description

The Examiner rejects claims 1-9 and 20 under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. The Examiner asserts that the specification fails to adequately describe the structural details of the elected compound.

Applicants traverse this rejection and submit that the specification reasonably conveys to a person skilled in the art at the time of filing that the Applicants' possessed the presently claimed subject matter, including the elected species currently under examination. The written description requirement may be satisfied by using "such descriptive means as *words*, structures, figures, diagrams, ***formulas***, etc., that fully set forth the claimed invention." *see Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Here, the specification has been amended to insert the detailed chemical formula of the presently elected compound. The specification incorporates by reference this compound, among

other related compounds, from copending International Application PCT/AU03/00427 (*see* page 1, lines 21-23).

Instead of relying on incorporation by reference of a foreign publication, Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. *See* M.P.E.P. §608.01(p) and 37 C.F.R. § 1.57(f). Here, the instant specification explicitly incorporates by reference the equol, dehydroequol, isofla-3-ene, and isoflavon compounds in copending International Application PCT/AU03/00427 (*see* page 1, lines 21-23 of the instant application), which describes the detailed chemical formula of the presently elected compound (*see* "compound 14" on page 26 of PCT/AU03/00427, or International Publication No. WO 2003/086386, enclosed herewith). As required, this chemical formula been inserted by specification amendment to overcome the written description rejection imposed by the Office. The material being inserted is the material incorporated by reference, such that the amendment contains no new matter. 37 C.F.R. § 1.57(f). Since the instant specification provides the detailed chemical structure of the presently elected compound, Applicants submit that the specification conveys to a person skilled in the art at the time of filing that Applicants possessed the presently claimed subject matter.

Applicants, therefore, submit that the instant claims satisfy the written description requirement under 35 U.S.C. § 112, first paragraph, and respectfully request withdrawal of this rejection.

Rejection Under 35 U.S.C. § 103

The Examiner rejects claims 1-2, 5-9 and 20 under 35 U.S.C. 103(a) for alleged obviousness over Kelley *et al.* (WO 98/08503), supported by Sinha *et al.* (*Photochem. Photobiol. Sci.*, 1:225-236 (2002)). The Examiner agrees that Kelly *et al.* do not teach a compound as presently elected, but asserts that Kelly *et al.* teach dehydroequol for the treatment of diseases associated with oxidant stress, including cancer and sunlight induced skin damage. In addition, the Examiner agrees that Kelly *et al.* do not specifically teach that the presently claimed compounds are capable of promoting metallothionein expression, but asserts that Kelly *et al.*

teach that such compounds are capable of scavenging free radicals. Since Sinha *et al.* teach that free radical formation following UV exposure is known to *induce* DNA damage through the formation of CPDs, the Examiner asserts that using a compound as taught in Kelly *et al.* would necessarily reduce the formation of CPDs, and thereby promote repair of UV-induced DNA damage.

Applicants respectfully traverse this rejection and submit that the instant claims satisfy the requirements of non-obviousness over the cited references. In particular, Applicants submit that the Examiner has not established a *prima facie* case of obviousness with respect to the presently claimed subject matter. *See In re Mayne*, 104 F.3d 1339 (Fed. Cir. 1997) (The USPTO has the burden of showing a *prima facie* case of obviousness). At a minimum, the Examiner must provide an explicit, apparent reason to combine these features in the fashion claimed by the Applicant with a reasonable expectation of success. *See KSR v. Teleflex, Inc.,* No. 04-1350 at 4, 14 (U.S. Apr. 30, 2007) ("A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art"). Here, the cited references, alone or ***in combination***, fail to motivate a person of ordinary skill in the art to reduce skin cancer formation with a reasonable expectation of success by applying a compound of claim 1 ***after*** UV exposure.

Neither Kelly *et al.* nor Sinha *et al.* motivate a person of ordinary skill in the art to reduce skin cancer formation with a reasonable expectation of success by applying a compound of claim 1 ***after*** UV exposure. In particular, Applicants respectfully disagree with the Examiner's assertion that the time course of treatment represents an obvious optimization step (*see* the Action, page 8). Applicants submit instead that topical application of the presently claimed compounds ***after*** UV exposure relates directly to the newly described properties of these compounds, including the ability to ***enhance the repair rate*** of damaged DNA, which properties are not described in either Kelly *et al.* or Sinha *et al.*

A person of ordinary skill in the art would not reasonably expect a compound having antioxidant activity alone (*i.e.* the ability to reduce free radical formation), as allegedly described in Kelly *et al.*, to provide therapeutic effects on reducing skin cancer formation when applied ***after*** UV exposure. More specifically, given the timing by which UV-induced free

radical formation relates to DNA mutagenic activity, a compound having antioxidant activity alone would not be expected to ***promote*** or ***enhance*** the repair rate of DNA mutagenic damage ***after*** UV exposure. As noted by the Examiner, free radical formation induces DNA damage through the formation of CPDs (*see* the Action, page 8). CPD formation occurs almost ***immediately*** upon UV exposure, representing the ***earliest*** indicator of molecular damage following exposure to UV radiation (*see, e.g.,* page 12, line 26). But after this ***immediate*** step of free radical-induced CPD formation, a compound understood to be capable of nothing more than *preventing* free radical *formation* via its antioxidant activity would be expected to have little, if any, further therapeutic effect once a subject is no longer exposed to UV light, such as ***after*** UV exposure. In other words, antioxidants may have been expected to prevent or reduce the *formation* of free radicals during exposure, but once the damage has already occurred and a subject is no longer exposed to UV radiation (*i.e.,* ***after*** UV exposure), such antioxidant compounds would have been expected to contribute little or nothing to the post-UV exposure repair process itself. Indeed, the Examiner has no technical basis to associate the *prevention* of free radical induced-CPD formation, as allegedly taught in Kelly *et al.*, with the enhancement of *the repair* of CPD formation, as would be necessary for a compound to provide significant therapeutic effects ***after*** UV exposure. As such, Kelly *et al.*, supported by Sinha *et al.*, fail to provide a person of ordinary skill in the art with the requisite motivation and reasonable expectation of success in applying the presently claimed compounds ***after*** UV exposure to increase the repair rate of skin cancer causing CPDs, and thereby reduce skin cancer formation.

In contrast, the instant application provides an apparent, technical reason for topically applying the recited genus of compounds ***after*** UV exposure. Indeed, a compound having the ability to actively *promote and/or enhance* the *repair rate* of DNA mutagenic damage, as empirically shown in the instant application (*see, e.g.,* Examples 2 and 3), would be expected to have a beneficial therapeutic effect on skin cancer formation when applied ***after*** UV exposure. In view of this understanding, and in view of the deficiencies in Kelly *et al.* and Sinha *et al.*, there is no suggestion to combine the teachings of these references, as advanced by the Examiner, except from using Applicants' invention as a template through a hindsight

reconstruction of Applicants' claims. *See Ex Parte Crawford et al.*, Appeal 20064249, Decided May 30, 2007.

Applicants submit that the cited references fail to provide either the requisite motivation or the requisite reasonable expectation of success in topically applying the genus of recited compounds ***after*** UV exposure to increase the repair rate of UV-induced DNA damage, and thereby reduce the formation of skin cancer. Given the deficiencies in the cited references, Applicants submit that the instant claims satisfy the requirements of non-obviousness under 35 U.S.C. § 103, and respectfully request withdrawal of this rejection.

Applicants respectfully submit that they believe that all of the claims in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

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